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Taiwanese Journal of Obstetrics & Gynecology 51 (2012) 596–602

www.tjog-online.com

Short Communication

Prenatal diagnosis of fetal multicystic dysplastic kidney in the era of three-dimensional ultrasound: 10-year experience

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Accepted 31 July 2012

Abstract

Objective: To demonstrate the usefulness of three-dimensional (3D) ultrasound in prenatal diagnosis of fetal multicystic dysplastic kidney (MCDK) disease.

Methods: In our previous study, we demonstrated that using 3D ultrasound in conjunction with traditional two-dimensional (2D) ultrasound can facilitate the diagnosis of MCDK. In this study, we followed all the MCDK cases diagnosed in our center in the recent decade (from 2002 to 2011) and compared the results with the data collected in the prior decade (from 1995 to 2002).

Results: Between 2002 and 2011, a total of 39 cases with fetal MCDK diagnosed by 2D and 3D ultrasound were retrospectively analyzed. The average gestational age when the diagnosis of MCDK was made was 23.6 weeks of gestation (95% confidence interval: 22.09–25.09). The Pearson chi-square test revealed a borderline nonsignificant difference statistically in the categorized gestational age at diagnosis ($p = 0.052$) as compared to the gestational age in the prior study. The average amniotic fluid index in fetuses with unilateral and bilateral MCDK was 16.76 ± 3.34 and 4.78 ± 5.82, respectively ($p < 0.001$). MCDK was not found to be associated with gestational age or chromosomal anomalies in our study.

Conclusion: The surface-rendering mode of 3D ultrasound is very useful in prenatal diagnosis and counseling for MCDK.

Keywords: multicystic dysplastic kidneys; prenatal diagnosis; three-dimensional ultrasound

Introduction

Multicystic dysplastic kidney (MCDK) is defined as a variant of renal dysplasia with multiple noncommunicating cysts separated by dysplastic parenchyma [1]. The overall incidence for unilateral MCDK is estimated to be approximately 1 in 4300 live births. Most MCDK are unilateral, with the left kidney more often affected (53.1%) [2]. In contrast, bilateral MCDK is a rare condition with a poor prognosis. Infants with bilateral kidney disease often die during the neonatal period [3]. Associated anomalies of the genitourinary tract with MCDK are common, including vesicoureteral reflux, urinary tract obstruction at the contralateral kidney, and abnormalities of the internal genitalia [4–6]. In addition, a variety of extrarenal associated abnormalities with MCDK had been reported, including congenital heart defects, central nervous system anomalies, spinal malformations, gastrointestinal malformations, single umbilical artery, omphalocele, abnormal extremities, and chromosomal anomalies [7]. Therefore, prenatal detection of MCDK is of importance in prenatal care.

Ultrasound (US) diagnosis for MCDK *in utero* has been undertaken for decades. The sensitivity for diagnosing MCDK by prenatal ultrasound ranged from 80% to 100% [8,9]. The classic features for MCDK on two-dimensional (2D) US are multiloculated intra-abdominal masses with multiple noncommunicating cysts. Normal renal parenchyma can hardly be

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1028-4559/$ - see front matter
http://dx.doi.org/10.1016/j.tjog.2012.09.015

identified between cystic walls. The affected kidney is usually enlarged with irregular contour under ultrasonography. The criteria for the diagnosis of MCDK were proposed to include echogenic renal parenchyma, multiple noncommunicating cysts with variable sizes at the periphery of the kidney, and no ultrasonic evidence of obstructive nephropathy [10].

In our previous study, we recommended that three-dimensional (3D) US could be used to facilitate the prenatal diagnosis of MCDK [11]. By using 3D US volume dataset, the examiner could reconstruct the region of interest, which may be missed or difficult to see during the 2D US examination [12]. Several advantages for using 3D US for the diagnosis of MCDK were well documented, which included vividly revealing the extent and severity of MCDK, shortening the scanning time for US examinations, and facilitating communications between physicians and patients by 3D reconstructed illustrations [11].

Our works on prenatal diagnosis of MCDK in a tertiary medical center from 1995 to 2002 by US were reported previously [11]. In this study, we followed up all prenatally diagnosed MCDK cases between 2002 and 2011,and compared the clinical characteristics with our previous report to comprehend the effect of 3D US on the diagnosis of MCDK.

Methods

Patients and setting

We undertook retrospective and consecutive research on prenatal diagnosis of MCDK, and reviewed all the cases with a diagnosis of MCDK by prenatal US in a tertiary medical center in Southern Taiwan from March 2002 to November 2011. Both 2D and 3D US were used for making the diagnosis of MCDK. The criteria applied for diagnosing MCDK on 2D US were as previously described [13]. Different 3D reconstruction modes were rendered to assist the diagnosis of MCDK. All the US examinations were performed in the Antenatal Ultrasound Laboratory, Department of Obstetrics and Gynecology, National Chang Kung University Hospital, Tainan, Taiwan. All the patients gave informed consent for US scanning and the study was approved by the Internal Review Board in our hospital.

US examination

The US machines used for the examinations were conventional 3D/4D ultrasound scanners, including Voluson 730 expert (General Electric Healthcare, Milwaukee, WI, USA) and Accuvix V20 (Medison, Seoul, Korea). The frequency used for scanning ranged from 3.5 Hz to 7.0 Hz. Detailed methods and modes of 3D US were as described previously [14–18]. In short, three orthogonal multiplanar views and 3D reconstruction images by various rendering modes were developed after 3D scanning (Fig. 1).

In addition, a level II fetal anatomic scan was performed in each case, and all associated abnormal findings besides MCDK were documented and recorded. An amniotic fluid index (AFI) was calculated according to the method described by Phelan et al [19] and an AFI less than 8.0 was considered as oligohydramnios.

Statistics

Statistical analyses were performed by the Statistical Package for Social Sciences (SPSS) version 17.0 (SPSS Inc., Chicago, IL, USA). Student t tests and Pearson chi-square tests were applied. A p value less than 0.05 was considered statistically significant.

Results

A total of 39 cases with unilateral or bilateral MCDK were included in our study between 2002 and 2011. The overall incidence for total MCDK was estimated to be 1 in 854 (0.117%, 39 per 33,306 prenatal ultrasound examinations). Most MCDKs are unilateral (87%, 34 of 39), and the right kidney more often affected (49%, 19 of 39). In addition, 38% (15 cases) of MCDK were on the left side, and 13% (5 cases) of MCDK were bilateral. The overall incidence for unilateral MCDK is estimated to be 1 in 980 (0.102%), and the overall incidence for bilateral MCDK is estimated to be 1 in 6667 (0.015%). All patients in our study were of Asian descent.

The characteristics for these cases are listed in Table 1. The average maternal age for patients with fetuses with MCDK diseases was 28.3 years (95% confidence interval: 26.7–29.9). The average gestational age when the diagnosis of MCDK was made was 23.6 weeks of gestation (95% confidence interval: 22.1–25.1). According to national regulations of prenatal ethics by our government, fetal sex identified by US was not documented in the database. Fourteen fetuses with MCDK were karyotyped by amniocentesis. Chromosome anomaly was found in only one case (7%) with balanced translocation [t(12,13)(p13:q21.2)]. The same chromosomal translocation was detected in the father of the fetus.

The average AFI in fetuses with unilateral MCDK (either left or right) and bilateral MCDK were 16.8 $\pm$ 3.3 and 4.8 $\pm$ 5.8, respectively (Table 3). The difference of AFI in unilateral and bilateral MCDK was significant statistically ($p < 0.001$). Oligohydramnios was found in four cases (10.3%); all of the cases were bilateral MCDK. In addition to MCDK, 16 cases (41%) were complicated with associated US anomalies, including echogenic intracardiac focus (9 of 39, 23.1%), dolicocephaly (1 of 39, 2.6%), echogenic bowel (1 of 39, 2.6%), cardiomegaly (1 of 39, 2.6%), diaphragmatic hernia (1 of 39, 2.6%), limb deformities (1 of 39, 2.6%), contralateral hydronephrosis (1 of 39, 2.6%), choroid plexus cyst (1 of 39, 2.6%), ureterovesical junction obstruction (1 of 39, 2.6%), cleft lip and palate (1 of 39, 2.6%), polydactyly (1 of 39, 2.6%), and short limbs (1 of 39, 2.6%).

To analyze the difference of prenatal diagnosis of MCDK in two decades, we compared our data in this series with the dataset from our previous report [11]. As listed in Table 2,

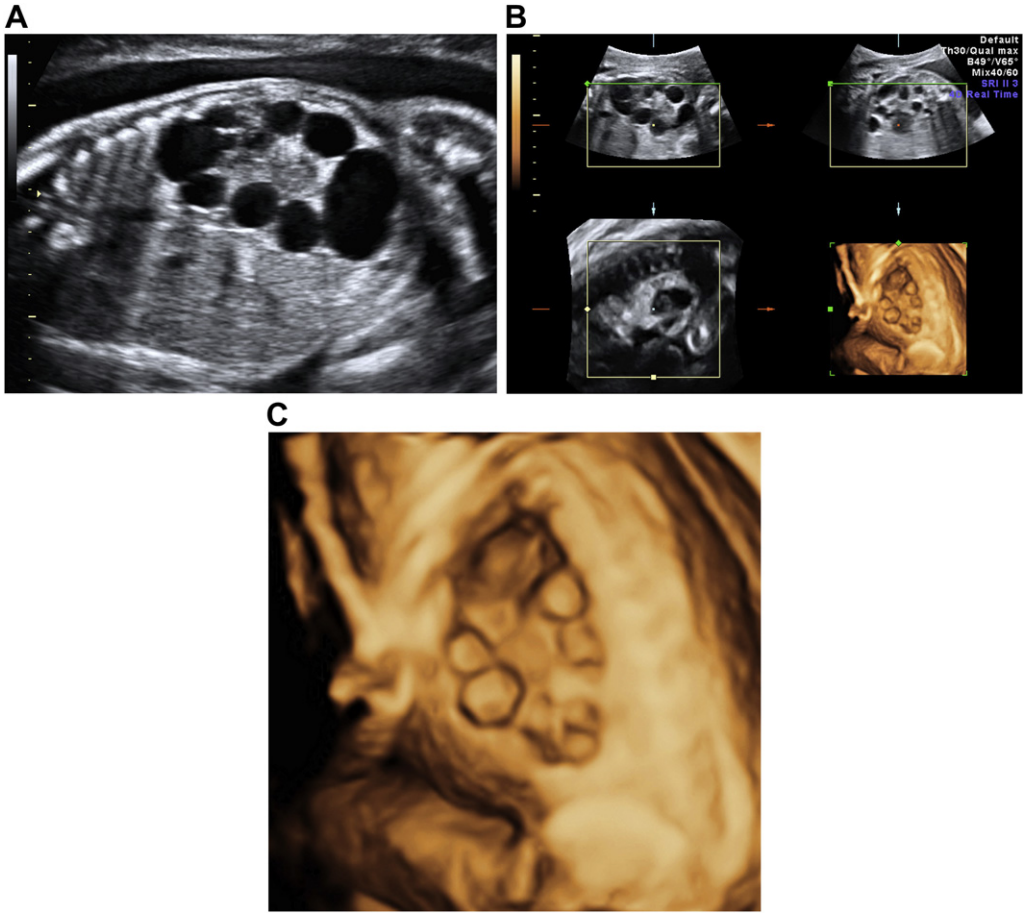

Fig. 1. The ultrasound images of multicystic dysplastic kidney (MCDK). (A) Traditional longitudinal view of MCDK by two-dimensional (2D) ultrasound (US). (B) Orthogonal multiplanar views and initial surface-rendered image of MCDK by 3D US. (C) Surface-rendering image of MCDK by 3D US.

there were a total of 28 MCDK cases in our prior study [11]. The mean maternal age with MCDK was 28.5 ± 4.5 years. The mean maternal ages had no significant difference statistically between two series ($p = 0.702$). In comparison with the gestational age at prenatal diagnosis of MCDK, no difference was observed statistically. Notably, we classified the gestational age of prenatal diagnosis into three trimesters. Pearson chi-square test revealed a borderline nonsignificant difference statistically in the trimesters of prenatal diagnosis of MCDK ($p = 0.052$).

Discussion

Incidence

In a meta-analysis incorporating 19 studies, the overall incidence of unilateral MCDK was calculated to be 1 in 4300 (ranging from 1 in 482 to 1 in 6753) [2]. In our study, the incidence for unilateral MCDK was estimated to be 1 in 980 (0.102%), which was close to the incidence reported in previous studies [20,21]. The reason why our reported incidence was above the average overall incidence of unilateral MCDK may be due to several factors. First, in this series, we calculated only the cases of MCDK detected prenatally. Second, we speculate that some fetuses with MCDK might be terminated prematurely, especially those fetuses with addition abnormalities on the contralateral kidney. Third, ethnic factors in different populations might be contributory to the difference of incidence. Hence, these factors might cause the difference in incidence of MCDK between our population and other foreign series. To compare the incidence of MCDK in different populations, further international collaboration investigations are needed.

Maternal age and obstetric history

The average maternal age for carrying a fetus with MCDK has had no obvious change in the past two decades. The point estimates for the mean maternal age in our study and the prior report were close to each other (28.5 and 28.3 years, respectively). Of the 39 cases, 18 (46.2%) were multiparous. There was no prior pregnancy with MCDK in all 18 multiparous patients. These results were compatible with those in our previous report [11], suggesting a nonhereditary feature of MCDK.

Gestational age at diagnosis

In the era of 3D US technology, we are expecting an early diagnosis for fetal anomalies in every aspect. In this study, the gestational age for the diagnosis of MCDK being made was

Table 1
Clinical characteristics for the MCDK cases in 2002–2011.

Case	Maternal age (y)	Pregnancy history	GA at Dx (wk)	AFI (cm)	Associated findings	Karyotype	Status of MCDK
1	21	G1P0	17	2.9	EB, oligohydramnios	—	Bilateral
2	30	G1P0	17	18.9	L UVJ obstruction	—	L
3	17	G1P0	18	14.9	—	—	R
4	30	G2P1	18	13.9	Bilateral CPC	—	R
5	26	G1P0	19	17.2	—	—	L
6	28	G1P0	20	12.6	EIF (LV)	—	R
7	31	G1P0	20	21.2	—	—	R
8	28	G4P2SA1	20	16.4	EIF (LV)	46, XX	L
9	24	G1P0	20	16.4	Cleft lip, cleft palate	—	R
10	27	G2P1	20	17.2	EIF (LV)	46, XY	R
11	24	G1P0	21	19.9	EIF (LV)	—	R
12	32	G1P0	21	13.9	—	—	L
13	29	G1P0	21	16.0	—	46, XX	R
14	31	G2P1	21	16.4	—	—	R
15	29	G2P1	21	17.2	—	46, XX	R
16	23	G1P0	22	2.0	EIF (LV), oligohydramnios, dolicocephaly	46, XY	Bilateral
17	29	G2P1	22	0.5	Oligohydramnios	46, XY	Bilateral
18	27	G1P0	22	N/A	EIF (LV)	—	R
19	30	G2P1	22	19.1	—	—	R
20	27	G2P1	22	13.6	EIF (LV)	—	R
21	37	G2P1	23	17.5	EIF (LV)	46, XX	R
22	41	G5P2AA3	23	3.5	Oligohydramnios, cardiomegaly	—	Bilateral
23	24	G2P0AA1	23	22.1	—	—	L
24	35	G2P1	23	16.8	Polydactyly, short limbs, EIF (LV)	46, XY	L
25	32	G2P1	23	15.6	—	—	R
26	29	G1P0	24	15.6	—	—	L
27	31	G1P0	24	15.4	—	46, XY[a]	L
28	25	G1P0	25	12.0	—	46, XX	R
29	19	G2P1	25	11.0	—	—	L
30	30	G2P1	27	19.0	—	—	R
31	28	G2P1	28	16.7	—	—	L
32	30	G1P0	28	23.0	—	46, XX	L
33	29	G2P0SA1	29	18.3	—	46, XX	R
34	37	G3P2	29	26.3	DH, R limbs deformities	46, XX	L
35	28	G2P1	30	15.0	R hydronephrosis	46, XY	Bilateral
36	20	G1P0	30	12.2	—	—	R
37	23	G1P0	32	18.1	—	—	L
38	29	G2P1	34	12.4	—	—	L
39	33	G3P0SA2	36	16.1	R hydronephrosis	—	L

AFI = amniotic fluid index; CPC = choroid plexus cyst; DH = diaphragmatic hernia; Dx = diagnosis; EB = echogenic bowel; EIF = echogenic intracardiac focus; GA = gestational age; L = left; LV = left ventricle; MCDK = multicystic dysplastic kidney; N/A = not available; R = right; UVJ = ureterovesical junction.
[a] 46, XY, t(12,13)(p13:q21.2).

improved nonsignificantly in the past decade in comparison with our previous report. Several factors could contribute to this result. First, the relatively small sample size may limit our ability to demonstrate a significant difference statistically.

Second, our study patients were from a single tertiary medical center where most of the cases were referred from primary care physicians. The gestational age at diagnosis was therefore highly dependent on the time when the patients were referred to our center. In other words, whether the primary care physicians or obstetricians had the facility to detect MCDK at an early gestational age is a pivotal factor to achieve an early diagnosis. It is worthwhile to mention that, for all the

Table 2
The comparison between two series.

	N	Maternal age at Dx	GA at Dx				
		Mean ± SD (y)	Mean ± SD (wk)	Dx at 1T	Dx at 2T	Dx at 3T	Chi- square test [b]
Prior series 1995–2002 [11]	28	28.5 ± 4.5	26.9 ± 5.5	0	17	11	0.052
This series 2002–2011	39	28.3 ± 4.9	23.6 ± 4.6	0	32	7	
p[a]		0.702	0.208				

Dx = diagnosis; GA = gestational age; SD = standard deviation; 1T = first trimester; 2T = second trimester; 3T = third trimester.
[a] Student t test; [b] Pearson chi-square test.

Table 3
The comparison of AFI.

MCDK	N	AFI (cm)	p[a]
		Mean ± SD	
Unilateral	34	16.8 ± 3.3	<0.001
Bilateral	5	4.8 ± 5.8	

AFI = amniotic fluid index; MCDK = multicystic dysplastic kidney.
[a] Student t test.

MCDK cases referring from other medical facilities, the diagnosis of MCDK was made on their first visit to our center.

Third, the nature of the disease itself plays a vital role in determining when it could be discovered. In the case of MCDK, it is proposed that the dysplastic kidney is originated from the improper ureteric canalization at approximately 8 weeks of gestation [22]. Starting from the 5th week of gestation, the ureteric bud grows from the mesonephric duct into the metanephric blaastema and marks the development of normal kidneys. The ureteric bud then branches and differentiates into the collecting ducts and ureter [3]. A primary ureteric bud defect leading to the branching and mesenchymal induction failure was proposed to cause MCDK [2]. The severity of the disease was thought to depend on the timing of the obstruction developed during nephrogenesis [7]. The timing of the disturbances of nephrogenesis would therefore determine the time when the dysplastic cystic kidney became overt under US, usually at about 20 weeks of gestation [11]. Hence, even though we are hoping that advanced technology would make an earlier diagnosis for MCDK possible, a natural limit may eliminate the possibility.

Unilateral or bilateral

In unilateral MCDK in our study, a slightly higher proportion of right-sided MCDK (48.7%) was found in our study, which was contradicted in prior studies [2]. In a meta-analysis incorporating 67 studies for evaluating the side of MCDK, significantly more instances of MCDK were found on the left side (53.1%) [2]. The relatively small sample size in our study may explain the contradictory result.

Comparison of AFI

Aside from one case with missing data of AFI, all cases with unilateral MCDK had normal AFI values. As shown in Table 1, oligohydramnios was only found in bilateral MCDK cases in our series. In Table 3, the average AFI with bilateral MCDK was 4.8 ± 5.8, which is remarkably less than that with unilateral MCDK ($p < 0.001$). These findings suggested that in unilateral disease, as long as there was a normal contralateral kidney, the renal function could be compensated *in utero*. In addition, oligohydramnios and bilateral MCDK are two important indicators for poor prognosis [7].

Comparison of karyotyping

In our series, the MCDK does not seem correlated with specific genomic syndromes or abnormal karyotypes. For patients who underwent karyotype determination prenatally, only one abnormal karyotype was found in a total of 14 cases. This is consistent with previous reports in the medical literature [7,23]. The father of the fetus with an abnormal karyotype had also undergone karyotyping, and the same chromosomal translocation was found in the father's chromosomes. To date, no report in the literature demonstrated that this translocation found in our study [t(12,13)(p13:q21.2)]was associated with MCDK or other genomic syndromes. We inferred that the abnormal karyotype might be simply an incidental finding that coincided with the MCDK.

Comparison of associated anomalies

Some associated anomalies were found in conjunction with MCDK in our study. The most common was the echogenic intracardiac focus (EIF) (23.1%, 9 of 39). EIF was considered to be a soft marker of fetal aneuploidy [24]. As reported in the literature, the incidence of EIF in the general population ranged from 0.13% to 20% [24], with an incidence between 3% and 6.9% in larger series [25–28]. In our series, a higher incidence of EIF in fetuses with MCDK was noted. Because our population was solely of Asian descendants, we do expect a higher incidence of EIF in our series. It has been reported that maternal ethnicity is associated with the incidence of EIF, and a higher rate of EIF was found in several ethnicities, including Asian (6.9%) [29]. Nevertheless, the reported incidence is still much less than the incidence in our MCDK population. The association between EIF and MCDK remains unclear and further studies may be warranted.

The role of 3D US

In our previous study [11], we demonstrated that 3D US can not only help to confirm the diagnosis of MCDK, but also denote the extent of the disease. In addition, the 3D multiplanar orthogonal views and surface-rendering modes are technically independent, and the recorded results could be reviewed later by physicians and improve the accuracy of diagnosis. The average scanning time for acquisition of the targeted views was shorter while performing 3D than 2D US. Another vital advantage of 3D US is the easily comprehensive reconstructed illustrations. These reconstructed images could be used to facilitate the communication between medical staff and patients, and therefore improve the quality of medical consultations. All of these aforementioned factors were again verified to be true in our series.

In our recent 10-year experiences using 3D US together with high-resolution 2D US, we found that the most favorable aspect of 3D US in the diagnosis of MCDK was to achieve a better prenatal consultation. 3D surface renderings of the involved kidney were understandable, even for a layman without sufficient medical knowledge (Fig. 1). Most, if not all, of the parents in our study could appreciate the nature of the disease by looking at the images depicted by the surface-rendering technique. This technique was initially applied primarily on the evaluation of facial and limb anomalies, and

is now in widespread use for a variety of fetal body parts and some special syndromes [12]. In this series, we proved that it is also valuable using the 3D technique in illustrating MCDK. Further studies regarding the changes in the attitudes of parents with diseased fetuses before and after 3D US examinations are recommended to validate 3D US in the role of parental-fetal bonding.

Although 3D US is superior to 2D US in several aspects, the role of 2D US seems to be indispensable. Using 3D US alone has been reported to be insufficient in detecting fetal anomalies in high-risk groups [30]. Poor quality of the volume datasets was reported to be one reason making 3D US unreliable [31]. Therefore, although the 3D volume acquisition (especially automatic acquisition) is convenient and could potentially ameliorate the operator-dependent disadvantages of a conventional 2D US, we recommend that 2D US should not be abandoned in current settings. As stated in our report a decade ago [11], 2D and 3D US should not be mutually exclusive. Rather, 2D and 3D US are complementary to each other. In this series, we are further convinced that 2D and 3D US should be two major tools in prenatal diagnosis and genetic consultation.

Conclusion

Given the aforementioned results and discussion, prenatal diagnosis of congenital anomalies is one of the most important works in obstetrics and fetal medicine [32–40]. Antenatal assessment of fetal growth [41], including AFI [42], is also crucial in evaluating fetal well-being. Among them, prenatal diagnosis of MCDK is just one of the important aspects of modern obstetrics and fetal medicine.

Acknowledgments

We are grateful for the assistance from the staff of Antenatal Ultrasound Laboratory, National Cheng Kung University Hospital, Tainan, Taiwan. This series was supported in part by a grant from National Science Council, Executive Yuan, Taipei, Taiwan.

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